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? s pd98059 or (pd(w)98059) or pd184352 or (pd(w)184352) or u0126 or (u(w)0126)
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    1890716 PD
    4598 98059
    4593 PD(W) 98059
    112 PD184352
    1890716 PD
    42 184352
    42 PD(W) 184352
    3330 U0126
    4173618 U
    1190 0126
    859 U(W) 0126
S1 15641 PD98059 OR (PD(W) 98059) OR PD184352 OR (PD(W) 184352) OR
    U0126 OR (U(W) 0126)
? s treat?(5n) (cancer or cancers or tumor or tumors or carcinoma or malignan?)
Processing
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    1423552 CANCER
    164843 CANCERS
    1507731 TUMOR
    619261 TUMORS
    845756 CARCINOMA
    561947 MALIGNAN?
S2 342796 TREAT? (5N) (CANCER OR CANCERS OR TUMOR OR TUMORS OR
    CARCINOMA OR MALIGNAN?)
? s s1 and s2
    15641 S1
    342796 S2
S3 272 S1 AND S2
? s s3 and py<=2000
Processing
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    39790601 PY<=2000
S4 64 S3 AND PY<=2000
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...examined 50 records (50)
...completed examining records
S5 31 RD (unique items)
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    2228104 FACTOR
    1171 LETHAL(W) FACTOR
    124344 LETHAL
    2919235 FACTORS
    173 LETHAL(W) FACTORS
S1 1317 (LETHAL(W) FACTOR)OR (LETHAL(W) FACTORS)
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? s melanoma
S2 149745 MELANOMA
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? s s1 and s2
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    149745 S2
S3 10 S1 AND S2
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? rd
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...completed examining records
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S4 5 RD (unique items)
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0012533928 BIOSIS NO.: 2000000252241

Involvement of mitogen-activated protein kinase pathways in DENSPM-induced apoptosis of human **melanoma** cells

AUTHOR: Chen Ying (Reprint); Kramer D L (Reprint); Vujcic S (Reprint); Porter C W (Reprint)

AUTHOR ADDRESS: Roswell Park Institute, Buffalo, NY, USA\*\*USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting (41): p313 March, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000; 20000401

ISSN: 0197-016X

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Involvement of mitogen-activated protein kinase pathways in DENSPM-induced apoptosis of human **melanoma** cells

2000

...REGISTRY NUMBERS: PD-98059;

DESCRIPTORS:

0012554534 BIOSIS NO.: 2000000272847

Mitogen-activated protein kinase inhibitors block the oncostatin M induced detachment of A375 **melanoma** cells from monolayer cultures in vitro

AUTHOR: Ryan R E (Reprint)

AUTHOR ADDRESS: VA Med Ctr, Mountain States Med Research Inst, Boise, ID, USA\*\*USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting (41): p871 March, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000; 20000401

ISSN: 0197-016X

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Mitogen-activated protein kinase inhibitors block the oncostatin M induced detachment of A375 **melanoma** cells from monolayer cultures in vitro  
2000

5/3,K,AB/6 (Item 2 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
(c) 2005 BIOSIS. All rts. reserv.

0012745972 BIOSIS NO.: 200000464285

Antiproliferative effect of interleukin 1 (IL-1) is mediated by P38MAP  
kinase in human **melanoma** cells A375: Contribution of ERK1/2

AUTHOR: Hayashi H (Reprint); Itoh S (Reprint); Hattori T (Reprint);  
Yamamura T (Reprint); Takii T (Reprint); Chiba T (Reprint); Onozaki K  
(Reprint)

AUTHOR ADDRESS: Faculty of Pharmaceutical Sciences, Nagoya City University,  
3-1 Tanabe-dori, Mizuho-ku, Nagoya, 467-8603, Japan\*\*Japan

JOURNAL: Cytokine 11 (11): p929 Nov., 1999 1999

MEDIUM: print

CONFERENCE/MEETING: Seventh Annual Conference of the International Cytokine  
Society Hilton Head, South Carolina, USA December 5-9, 1999; 19991205

SPONSOR: The International Cytokine Society

ISSN: 1043-4666

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Antiproliferative effect of interleukin 1 (IL-1) is mediated by P38MAP  
kinase in human **melanoma** cells A375: Contribution of ERK1/2

1999

...REGISTRY NUMBERS: PD98059;

DESCRIPTORS:

...ORGANISMS: human **melanoma** cell line...

10541105 PMID: 10640428

Activation of integrin alpha(V)beta(3) regulates cell adhesion and migration to bone sialoprotein.

Byzova T V; Kim W; Midura R J; Plow E F

Joseph J. Jacobs Center for Thrombosis and Vascular Biology, Department of Molecular Cardiology, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44195, USA.

Experimental cell research (UNITED STATES) Feb 1 2000, 254 (2)

p299-308, ISSN 0014-4827 Journal Code: 0373226

Contract/Grant No.: HL54924; HL; NHLBI; RR-00080; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

alpha(V)beta(3), a broadly distributed member of the integrin family of adhesion receptors, has been implicated in a variety of physiological and pathophysiological events, including control of bone density, angiogenesis, apoptosis, tumor growth, and metastasis. Recently, it has been shown that activation of alpha(V)beta(3), its transition from a low- to a high-affinity/avidity state, influences its recognition of certain ligands. Bone sialoprotein (BSP) is recognized as an important ligand for alpha(V)beta(3) in processes ranging from bone formation to the homing of metastatic tumor cells. Here, the influence of alpha(V)beta(3) activation on the adhesion and migration of relevant cells to BSP has been examined. Stimulation of lymphoblastoid, osteoblastoid, and human umbilical vein endothelial cells (HUVEC) with PMA or Mn(2+) markedly enhanced alpha(V)beta(3)-dependent adhesion to BSP. alpha(V)beta(3)-mediated migration of HUVEC or osteoblastic cells to BSP was substantially enhanced by stimulation, demonstrating that alpha(V)beta(3) activation enhances both adhesive and migratory responses. However, adhesion and/or migration of certain tumor cell lines, including M21 melanoma and MDA MB435 and SKBR3 breast carcinoma cell lines, to BSP was constitutively high and was not augmented by alpha(V)beta(3)-activating stimuli. Inhibitors of the

```

?
PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
? s pd98059 or (pd(w)98059)or u0126 or (u(w)0126) or pd184352 or (pd(w)184352)
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    4598 98059
    4593 PD(W)98059
    3330 U0126
    4173618 U
    1190 0126
    859 U(W)0126
    112 PD184352
    1890716 PD
    42 184352
    42 PD(W)184352
S1 15641 PD98059 OR (PD(W)98059)OR U0126 OR (U(W)0126) OR PD184352
    OR (PD(W)184352)
? s melanoma
S2 149727 MELANOMA
? s s1 and s2
    15641 S1
    149727 S2
S3 132 S1 AND S2
? s s3 and py<=2000
Processing
    132 S3
    39790601 PY<=2000
S4 19 S3 AND PY<=2000
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>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
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5/3,K,AB/1 (Item 1 from file: 155)  
 DIALOG(R)File 155:MEDLINE(R)  
 (c) format only 2005 The Dialog Corp. All rts. reserv.

13852093 PMID: 9545341

Inhibition of the mitogen-activated protein kinase pathway triggers B16 melanoma cell differentiation.

Englaro W; Bertolotto C; Busca R; Brunet A; Pages G; Ortonne J P; Ballotti R

INSERM U-385, Faculte de medecine, Avenue de Valombrese, 06107 Nice Cedex 2, France.

Journal of biological chemistry (UNITED STATES) Apr 17 1998, 273

(16) p9966-70, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

In B16 melanoma cells, mitogen-activated protein (MAP) kinases are activated during cAMP-induced melanogenesis (Englaro, W., Rezzonico, R., Durand-Clement, M., Lallemand, D., Ortonne, J. P., and Ballotti, R. (1995) J. Biol. Chem. 270, 24315-24320). To establish the role of the MAP kinases in melanogenesis, we studied the effects of a specific MAP kinase kinase (MEK) inhibitor PD 98059 on different melanogenic parameters. We showed that PD 98059 inhibits the activation of MAP kinase extracellular signal-regulated kinase 1 by cAMP, but does not impair the effects of cAMP either on the morphological differentiation, characterized by an increase in dendrite outgrowth, or on the up-regulation of tyrosinase

that is the key enzyme in melanogenesis. On the contrary, PD 98059 promotes by itself cell dendricity and increases the tyrosinase amount and activity. Moreover, down-regulation of the MAP kinase pathway by PD 98059 , or with dominant negative mutants of p21(ras) and MEK, triggers a stimulation of the tyrosinase promoter activity and enhances the effect of cAMP on this parameter. Conversely, activation of the MAP kinase pathway, using constitutive active mutants of p21(ras) and MEK, leads to an inhibition of basal and cAMP-induced tyrosinase gene transcription. These results demonstrate that the MAP kinase pathway activation is not required for cAMP-induced melanogenesis. Furthermore, the inhibition of this pathway induces B16 melanoma cell differentiation, while a sustained activation impairs the melanogenic effect of cAMP-elevating agents.

Inhibition of the mitogen-activated protein kinase pathway triggers B16 melanoma cell differentiation.

Apr 17 1998,

In B16 melanoma cells, mitogen-activated protein (MAP) kinases are activated during cAMP-induced melanogenesis (Englaro, W., Rezzonico...  
... kinases in melanogenesis, we studied the effects of a specific MAP kinase kinase (MEK) inhibitor PD 98059 on different melanogenic parameters. We showed that PD 98059 inhibits the activation of MAP kinase extracellular signal-regulated kinase 1 by cAMP, but does...

...the up-regulation of tyrosinase that is the key enzyme in melanogenesis. On the contrary, PD 98059 promotes by itself cell dendricity and increases the tyrosinase amount and activity. Moreover, down-regulation of the MAP kinase pathway by PD 98059 , or with dominant negative mutants of p21(ras) and MEK, triggers a stimulation of the...

... is not required for cAMP-induced melanogenesis. Furthermore, the inhibition of this pathway induces B16 melanoma cell differentiation, while a sustained activation impairs the melanogenic effect of

Set	Items	Description
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S2	149727	MELANOMA
S3	132	S1 AND S2
S4	19	S3 AND PY<=2000
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	1423552	CANCER
	164843	CANCERS
	1507731	TUMOR
	619261	TUMORS
	845756	CARCINOMA
	561947	MALIGNAN?
S6	99309	COLON(5N) (CANCER OR CANCERS OR TUMOR OR TUMORS OR CARCINOMA OR MALIGNAN?)
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	99309	S6
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Processing		
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>>>Duplicate detection is not supported for File 340.		
>>>Records from unsupported files will be retained in the RD set.		
...completed examining records		
S9	24	RD (unique items)

06055002    Genuine Article#: XR765    Number of References: 37  
 Title: Characterization of the antiproliferative signal mediated by the  
       somatostatin receptor subtype sst5 (ABSTRACT AVAILABLE)  
 Author(s): Cordelier P; Esteve JP; Bousquet C; Delesque N; OCarroll AM;  
       Schally AV; Vaysse N; Susini C; Buscail L (REPRINT)  
 Corporate Source: CHU RANGUEIL, INST LOUIS BUGNARD, INSERM, U151, 1 AVE J  
       POULHES/F-31403 TOULOUSE 04//FRANCE/ (REPRINT); CHU RANGUEIL, INST LOUIS  
       BUGNARD, INSERM, U151/F-31403 TOULOUSE 04//FRANCE/;  
       NIMH,/BETHESDA//MD/20892; TULANE UNIV, SCH MED/NEW ORLEANS//LA/70112;  
       VET AFFAIRS MED CTR,/NEW ORLEANS//LA/70112  
 Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED  
       STATES OF AMERICA, 1997, V94, N17 (AUG 19), P9343-9348  
 ISSN: 0027-8424    Publication date: 19970819  
 Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC  
       20418

Language: English    Document Type: ARTICLE

Abstract: We investigated cell proliferation modulated by cholecystokinin  
 (CCK) and somatostatin analogue RC-160 in CHO cells bearing endogenous  
 CCKA receptors and stably transfected by human subtype sst5  
 somatostatin receptor, CCK stimulated cell proliferation of CHO cells,  
 This effect was suppressed by inhibitor of the soluble guanylate  
 cyclase, LY 83583, the inhibitor of the cGMP dependent kinases, KT  
 5823, and the inhibitor of mitogen-activated protein (MAP) kinase  
 kinase, PD 98059, CCK treatment induced an increase of  
 intracellular cGMP concentrations, but concomitant addition of LY 83583  
 virtually suppressed this increase, CCK also activated both  
 phosphorylation and activity of p42-MAP kinase; these effects were  
 inhibited by KT 5823. All the effects of CCK depended on a pertussis  
 toxin-dependent G protein. Somatostatin analogue RC-160 inhibited  
 CCK-induced stimulation of cell proliferation but it did not potentiate  
 the suppressive effect of the inhibitors LY 83583 and KT 5823. RC-160  
 inhibited both CCK-induced intracellular cGMP formation as well as  
 activation of p42-MAP kinase phosphorylation and activity, This  
 inhibitory effect was observed at doses of RC-160 similar to those  
 necessary to occupy the sst5 recombinant receptor and to inhibit  
 CCK-induced cell proliferation, We conclude that, in CHO cells, the  
 proliferation and the MAP kinase signaling cascade depend on a  
 cGMP-dependent pathway, These effects are positively regulated by CCK  
 and negatively influenced by RC-160. interacting through CCKA and sst5  
 receptors, respectively, These studies provide a characterization of  
 the antiproliferative signal mediated by sst5 receptor.

, 1997

...Abstract: cGMP dependent kinases, KT 5823, and the inhibitor of  
 mitogen-activated protein (MAP) kinase kinase, PD 98059,  
 CCK treatment induced an increase of intracellular cGMP concentrations,  
 but concomitant addition of LY 83583...

...Identifiers--ACTIVATED PROTEIN-KINASE; PANCREATIC ACINAR-CELLS; HUMAN-  
**COLON CANCER**; TYROSINE PHOSPHATASE; ANALOG RC-160; IN-VIVO;  
 GROWTH; PROLIFERATION; RAT; INHIBITION

? s log off

      S10            0    LOG OFF

? log off

      21jan05 09:52:14 User231882 Session D1386.3  
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\$19.06 0.861 DialUnits File434  
\$19.06 Estimated cost File434  
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\$5.25 TELNET  
\$175.36 Estimated cost this search  
\$175.44 Estimated total session cost 6.713 DialUnits  
Logoff: level 04.20.00 D 09:52:14

IALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2005 Inst for Sci Info. All rts. reserv.

06094597 Genuine Article#: XU769 Number of References: 126  
Title: Inhibitors of Ras-transformation (ABSTRACT AVAILABLE)  
Author(s): Sugita K; Ohtani M  
Corporate Source: SHIONOGI & CO LTD, SHIONOGI RES LABS, FUKUSHIMA KU/OSAKA  
553//JAPAN/

Journal: CURRENT PHARMACEUTICAL DESIGN, 1997, V3, N3 (JUN), P323-334  
ISSN: 1381-6128 Publication date: 19970600  
Publisher: BENTHAM SCIENCE PUBL BV, PO BOX 75676, 1118 ZS SCHIPHOL,  
NETHERLANDS

Language: English Document Type: REVIEW

Abstract: Ras-oncogene is now thought to be one of the most important  
oncogenes which is evidenced in the correlation with human cancers.  
Point mutation in ras-gene correlates with transformation caused by ras  
and is found in human cancers with high frequency, such as 90% in  
pancreatic cancer, 50% in colon cancer and 30% in  
lung cancer. Ras (product of ras-oncogene) has GTPase activity  
and loses its activity with point mutation, leading to transformation.  
Active CTP-binding form of Ras is a key molecule of signal transduction  
in cell growth, differentiation and transformation.

Inhibitors of ras-transformation will be good candidates of  
anti-cancer agents. Although many inhibitors of ras-transformation have  
been reported up to now including macromolecules (genes, nucleotides,  
antibodies), we summarize the small-molecule compounds, which inhibit  
ras-transformation in direct or indirect manner in this review. Direct  
inhibitors of ras include inhibitors of farnesylation of Ras.  
Farnesyltransferase inhibitors (L-744,832, etc) include peptidomimetics  
with the rational drug design for C-terminus of Rns and natural  
products. Inhibitors of 3-hydroxy-3-methyl-glutaryl coenzyme A  
(HMG-CoA) reductase (Lovastatin, etc) which block cholesterol  
metabolism, inhibit farnesylation of Ras by decreasing the amount of  
the substrate of farnesyltransferase (FTase). Indirect inhibitors of  
ras with known mechanisms include the inhibitor of inositol  
monophosphate (IMP) dehydrogenase (oxanosine), the inhibitor of  
mitogen-activated protein kinase kinase (MAPK kinase) (PD98059),  
the inhibitor of MAPK (apigenin), the inhibitors of protein kinase C  
(PKC) (UCN-01, etc), the inhibitors of phosphatidylinositol 3-kinase  
(PI3K) (Wortmannin and L-294002), the inducer of the transcription  
factor JunD (oxamflatin) and the inhibitors of histone deacetylase  
[trichostatin A (TSA) and trapoxins]. Almost all compounds are now  
under development, and will be evaluated in clinical studies as  
anticancer agents.

, 1997

...Abstract: ras and is found in human cancers with high frequency, such as  
90% in pancreatic cancer, 50% in colon cancer and 30%  
in lung cancer. Ras (product of ras-oncogene) has GTPase activity  
and loses its activity with point mutation...

...inositol monophosphate (IMP) dehydrogenase (oxanosine), the inhibitor of  
mitogen-activated protein kinase kinase (MAPK kinase) (PD98059),  
the inhibitor of MAPK (apigenin), the inhibitors of protein kinase C  
(PKC) (UCN-01, etc...

9/3,K,AB/24 (Item 6 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2005 Inst for Sci Info. All rts. reserv.

06055002 Genuine Article#: XR765 Numbe

08566033    Genuine Article#: 301TG    Number of References: 55

Title: EGF stimulates gastrin promoter through activation of Sp1 kinase activity (ABSTRACT AVAILABLE)

Author(s): Chupreta S; Du M; Todisco A; Merchant JL (REPRINT)

Corporate Source: MSRB I,1150 W MED DR, 3510/ANN ARBOR//MI/48109 (REPRINT);  
UNIV MICHIGAN,DEPT INTERNAL MED/ANN ARBOR//MI/48109; UNIV MICHIGAN,DEPT  
PHYSIOL/ANN ARBOR//MI/48109; UNIV MICHIGAN,HOWARD HUGHES MED INST/ANN  
ARBOR//MI/48109

Journal: AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY, 2000, V278,  
N4 (APR), PC697-C708

ISSN: 0363-6143    Publication date: 20000400

Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814

Language: English    Document Type: ARTICLE

Abstract: Epidermal growth factor (EGF) receptor activation stimulates gastrin gene expression through a GC-rich element called gastrin EGF response element (gERE). This element is bound by Sp1 family members and is a target of the ras-extracellular signal-regulated kinase (Erk) signal transduction cascade. This raised the possibility that Sp1 may be phosphorylated by kinases of this signaling pathway. Erk is capable of phosphorylating other mitogen-inducible transcription factors, e.g., Elk and Sap, suggesting that Erk may also mediate EGF-dependent phosphorylation of Sp1. This possibility was tested by studying Sp1-dependent kinase activity in extracts prepared from EGF-activated AGS cells by use of solid-phase kinase assays and immunoprecipitation of metabolically labeled Sp1. The results revealed that Sp1 kinase activity (like gastrin promoter activation) is inhibited by PD-98059 and, therefore, is dependent on mitogen-activated protein kinase kinase 1 (Mek 1). However, EGF-dependent activation of endogenous Erk did not account for most of the Sp1 kinase activity, since Erk and additional Sp1 kinase activity analyzed in a solid-phase kinase assay eluted from an ion-exchange column in different fractions. Phosphoamino acid analysis of in vivo radiolabeled Sp1 demonstrated that the kinase phosphorylates Sp1 on Ser and Thr in response to EGF. Therefore, most EGF-stimulated Sp1 kinase activity is Mek 1 dependent and distinct from Erk.

, 2000

...Abstract: Sp1. The results revealed that Sp1 kinase activity (like gastrin promoter activation) is inhibited by PD-98059 and, therefore, is dependent on mitogen-activated protein kinase kinase 1 (Mek 1). However, EGF...

0012556984 BIOSIS NO.: 200000275297

Mirk is a MAP kinase substrate upregulated in **colon cancers**

AUTHOR: Deng Xiaobing (Reprint); Lee K (Reprint); Friedman E (Reprint)

AUTHOR ADDRESS: Upstate Med Univ, Syracuse, NY, USA\*\*USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting (41): p714 March, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000; 20000401

ISSN: 0197-016X

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Mirk is a MAP kinase substrate upregulated in **colon cancers**  
2000

...REGISTRY NUMBERS: **PD98059**

DESCRIPTORS:

DISEASES: **colon cancer--**

CHEMICALS & BIOCHEMICALS: ...**PD98059--**

0552493 PMID: 10655059

A genome-wide survey of RAS transformation targets.

Zuber J; Tchernitsa O I; Hinzmann B; Schmitz A C; Grips M; Hellriegel M; Sers C; Rosenthal A; Schafer R

[1] Laboratory of Molecular Tumour Pathology, Institute of Pathology, Charite, Humboldt-University D-10117, Berlin, Germany.

Nature genetics (UNITED STATES) Feb 2000, 24 (2) p144-52, ✓

ISSN 1061-4036 Journal Code: 9216904

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

An important aspect of multi-step tumorigenesis is the mutational activation of genes of the RAS family, particularly in sporadic **cancers** of the pancreas, colon, lung and myeloid system. RAS genes encode small GTP-binding proteins that affect gene expression in a global way by acting as major switches in signal transduction processes, coupling extracellular signals with transcription factors. Oncogenic forms of RAS are locked in their active state and transduce signals essential for transformation, angiogenesis, invasion and metastasis via downstream pathways involving the RAF/MEK/ERK cascade of cytoplasmic kinases, the small GTP-binding proteins RAC and RHO, phosphatidylinositol 3-kinase and others. We have used subtractive suppression hybridization (SSH), a PCR-based cDNA subtraction technique, to contrast differential gene expression profiles in immortalized, non-tumorigenic rat embryo fibroblasts and in HRAS-transformed cells. Sequence and expression analysis of more than 1,200 subtracted cDNA fragments revealed transcriptional stimulation or repression of 104 ESTs, 45 novel sequences and 244 known genes in HRAS-transformed cells compared with normal cells. Furthermore, we identified common and distinct targets in cells transformed by mutant HRAS, KRAS and NRAS, as well as 61 putative target genes controlled by the RAF/MEK/ERK pathway in reverted cells treated with the MEK-specific inhibitor PD 98059.

4100306 PMID: 9797369

Oncogenic ras induces gastrin gene expression in **colon cancer**

Nakata H; Wang S L; Chung D C; Westwick J K; Tillotson L G

Division of Digestive Diseases and Nutrition, Department of Medicine,  
University of North Carolina, Chapel Hill, North Carolina, USA.

Gastroenterology (UNITED STATES) Nov 1998, 115 (5) p1144-53,

ISSN 0016-5085 Journal Code: 0374630

Contract/Grant No.: P30DK34987; DK; NIDDK; R29 DK49860; DK; NIDDK

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

**BACKGROUND & AIMS:** The expression of gastrin, as a tumor growth factor, is significantly increased in some **colon cancers** compared with the low levels found in normal mucosa. The aim of this study was to elucidate the transcriptional mechanisms of gastrin induction in **colon cancer**. **METHODS:** Gastrin messenger (mRNA) levels and K-ras genotype were determined in **colon cancer** cell lines and surgical specimens. **Colon cancer** cells were transfected with oncogenic ras expression vectors, and transcriptional activity was assayed with gastrin-luciferase reporter genes. **RESULTS:** **Colon cancer** cell lines and tissues with K-ras mutations all had significantly higher gastrin mRNA levels than those that were ras wild type. Treatment of several ras mutant cell lines with **PD98059**, an inhibitor of mitogen-activated protein kinase kinase, resulted in a decrease in endogenous gastrin mRNA levels. The effects of ras on gastrin expression appeared to be mediated through the gastrin promoter because transfection of oncogenic ras and activated raf expression vectors both induced gastrin-promoter, luciferase-reporter genes. The inductive effects of oncogenic ras could be blocked by the coexpression of dominant negative forms of raf and extracellular regulated kinase. **CONCLUSIONS:** Oncogenic ras

9/3,K,AB/2 (Item 2 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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14487002 PMID: 10484389

Requirement of the MAP kinase cascade for cell cycle progression and differentiation of human intestinal cells.

Aliaga J C; Deschenes C; Beaulieu J F; Calvo E L; Rivard N  
Groupe du Conseil de Recherches Medicales sur le Developpement Fonctionnel et la Physiopathologie du Tube Digestif, Departement d'Anatomie et Biologie Cellulaire, Faculte de Medecine, Universite de Sherbrooke, Sherbrooke, Quebec, Canada.

American journal of physiology (UNITED STATES) Sep 1999, 277 (3  
Pt 1) pG631-41, ISSN 0002-9513 Journal Code: 0370511

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The intracellular signaling pathways responsible for cell cycle arrest and establishment of differentiated cells along the gut axis remain largely unknown. In the present study, we analyzed the regulation of p42/p44 mitogen-activated protein kinase (MAPK) in the process of proliferation and differentiation of human intestinal cells. In vitro studies were done in Caco-2/15 cells, a human colon cancer cell line that spontaneously differentiates into an enterocyte phenotype. In vivo studies were performed on cryostat sections of human fetal intestinal epithelium by indirect immunofluorescence. We found that inhibition of the p42/p44 MAPK signaling by the PD-98059 compound or by ectopic expression of the MAPK phosphatase-1 strongly attenuated E2F-dependent transcriptional activity in Caco-2/15 cells. p42/p44 MAPK activities dramatically decreased as soon as Caco-2/15 cells reached confluence. However, significant levels of activated p42 MAPK were detected in differentiated Caco-2/15 cells. Addition of PD-98059 during differentiation interfered with sustained activation of p42 MAPK and sucrase-isomaltase expression. Although p42/p44 MAPKs were expressed in both the villus tip and crypt cells, their phosphorylated and active forms were detected in the undifferentiated crypt cells. Our results indicate that elevated p42/p44 MAPK activities stimulate cell proliferation of intestinal cells, whereas low sustained levels of MAPK activities correlated with G1 arrest and increased expression of sucrase-isomaltase.

Sep 1999,

...human intestinal cells. In vitro studies were done in Caco-2/15 cells, a human colon cancer cell line that spontaneously differentiates into an enterocyte phenotype. In vivo studies were performed on...

... by indirect immunofluorescence. We found that inhibition of the p42/p44 MAPK signaling by the PD-98059 compound or by ectopic expression of the MAPK phosphatase-1 strongly attenuated E2F-dependent transcriptional...

... levels of activated p42 MAPK were detected in differentiated Caco-2/15 cells. Addition of PD-98059 during differentiation interfered with sustained activation of p42 MAPK and sucrase-isomaltase expression. Although p42...

9/3,K,AB/3 (Item 3 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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14408249 PMID: 10404512

Glycine-extended gastrin exerts growth-promoting effects on human

colon cancer cells.

Stepan V M; Sawada M; Todisco A; Dickinson C J  
Department of Pediatrics, University of Michigan, Medical Center, Ann Arbor 48109-0658, USA.

Molecular medicine (Cambridge, Mass.) (UNITED STATES) Mar 1999,

5 (3) p147-59, ISSN 1076-1551 Journal Code: 9501023

Contract/Grant No.: KO8DK02336; DK; NIDDK; RO1DK34306; DK; NIDDK; RO1DK47398; DK; NIDDK; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: Since human colon cancers often contain significant quantities of progastrin-processing intermediates, we sought to explore the possibility that the biosynthetic precursor of fully processed amidated gastrin, glycine-extended gastrin, may exert trophic effects on human colonic cancer cells. MATERIALS AND METHODS: Binding of radiolabeled glycine-extended and amidated gastrins was assessed on five human cancer cell lines: LoVo, HT 29, HCT 116, Colo 320DM, and T 84. Trophic act

5/3,K,AB/3 (Item 3 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
(c) format only 2005 The Dialog Corp. All rts. reserv.

14426723 PMID: 10424744

PD 098059, an inhibitor of ERK1 activation, attenuates the in vivo invasiveness of head and neck squamous cell carcinoma.

Simon C; Hicks M J; Nemechek A J; Mehta R; O'Malley B W; Goepfert H; Flaitz C M; Boyd D

Department of Head and Neck Surgery, The University of Texas, MD Anderson Cancer Center, Houston 77030, USA.

British journal of cancer (SCOTLAND) Jul 1999, 80 (9) p1412-9,  
ISSN 0007-0920 Journal Code: 0370635

Contract/Grant No.: P50 DE11906; DE; NIDCR; ROI CA58311; CA; NCI; ROI DE10845; DE; NIDCR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Increased mortality of patients with oral cancer largely reflects the local and regional spread of the disease. The invasiveness of these tumours requires hydrolases which are regulated through AP-1-dependent transcriptional mechanisms. Since the amount/activity of transcription factors bound to the AP-1 motif are regulated partly through the extracellular signal-regulated kinases (ERK1/ERK2), we determined the effect of PD 098059, an inhibitor of ERK1/ERK2 activation, on the in vivo invasiveness of a human squamous cell carcinoma cell line (UM-SCC-1) derived from the oral cavity. We utilized the floor of mouth musculature consisting of the mylohyoid, geniohyoid and genioglossus muscle (which are sequentially arranged), as a natural barrier to assess tumour spread in vivo in the nude mouse. Mice were inoculated with tumour cells superficial to the mylohyoid muscle. After 18 days, tumours were injected with either empty liposomes (control) or liposomes containing 5 microm PD 098059 and, after an additional 22 days, the jaws of mice examined histologically. Highly infiltrative tumours, which had penetrated the genioglossus muscle, were evident in 10/12 control mice. In contrast, in 9/12 mice in which the tumours were injected with PD 098059, tumours did not extend beyond the mylohyoid or geniohyoid muscles. Tumours penetrated bone nutrient canals in 7/12 control mice but in only 3/12 PD 098059-treated mice. Neurotropism, characteristic of aggressive oral squamous cell carcinoma, was evident in 6/12 control mice but was completely abolished (0/12 mice) in the PD 098059-treated mice. Using a staging system based on the muscle layer involved, neurotropism, as well as bone involvement, we found the inhibition of invasion to be statistically significant ( $P < 0.01$ ). The reduced invasiveness of the PD 098059-liposome-treated oral cancers was associated with diminished 92-kDa type IV collagenase and ERK1/ERK2 activities but was not a consequence of a slower tumour growth rate. This is the first study to demonstrate reduced in vivo invasiveness of a malignancy brought about by an inhibitor of ERK1/ERK2 activation. These results raise the exciting possibility that second generation PD 098059 congeners may reduce the spread of the disease in patients afflicted with oral cancers.

Jul 1999,

... to be statistically significant ( $P < 0.01$ ). The reduced invasiveness of the PD 098059-liposome-treated oral cancers was associated with diminished 92-kDa type IV collagenase and ERK1/ERK2 activities but was ...

Chemical Name: Enzyme Inhibitors; Flavonoids; PD 98059;  
1,2-Dipalmitoylphosphatidylcholine; Ca(2+)-Calmodulin Dependent Protein Kinase; Mitogen-Activated Protein Kinases; extracellular signal...

5/3,K,AB/4 (Item 4 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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14359253 PMID: 10355747

Effects of bombesin on methadone-induced apoptosis of human lung cancer cells.

Heusch W L; Maneckjee R

Division of Surgical Oncology, Oregon Health Sciences University, Portland 97201-3098, USA.

Cancer letters (IRELAND) Mar 1 1999, 136 (2) p177-85, ISSN

0304-3835 Journal Code: 7600053

Contract/Grant No.: CA 59037; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The therapeutic opioid methadone, used to treat cancer pain and opioid addiction, is also a potent inducer of apoptosis in human lung cancer cells, thereby inhibiting their growth. However, in contrast to its central nervous system (CNS) actions, this effect appears to be mediated through a non-opioid mechanism involving bombesin, an autocrine growth-stimulatory factor that plays a central role in the early events of pulmonary carcinogenesis. Exposure of 'variant' small cell lung carcinoma (SCLC) and non-SCLC cells, which secrete low concentrations ( $< 0.01$  pmol/mg protein) of bombesin, to nanomolar concentrations of methadone resulted in increased levels of mitogen-activated protein (MAP) kinase phosphatases and inactivation of MAP kinase, suppression of the bcl-2 protein, and induction of apoptosis. These effects of methadone were reversed by the addition of bombesin to the culture medium, at concentrations of  $< 1$  microm, and 'classic' SCLC cells, which secrete high concentrations of bioactive bombesin ( $> 6$  pmol/mg protein), were found not to respond to methadone. Thus, methadone's effectiveness is dependent upon the concentration of bioactive bombesin secreted by lung cancer cells. Methadone

08927314    Genuine Article#: 345XM    Number of References: 45

Title: Blockade of the epidermal growth factor receptor tyrosine kinase suppresses tumorigenesis in MMTV/Neu plus MMTV/TGF-alpha bigenic mice (ABSTRACT AVAILABLE)

Author(s): Lenferink AEG; Simpson JF; Shawver LK; Coffey RJ; Forbes JT; Arteaga CL (REPRINT)

Corporate Source: VANDERBILT UNIV,SCH MED, DIV ONCOL, 22ND AVE SOUTH, 1956 TVC/NASHVILLE//TN/37232 (REPRINT); VANDERBILT UNIV,SCH MED, DEPT MED/NASHVILLE//TN/37232; VANDERBILT UNIV,SCH MED, DEPT CELL BIOL/NASHVILLE//TN/37232; VANDERBILT UNIV,SCH MED, DEPT PATHOL/NASHVILLE//TN/37232; DEPT VET AFFAIRS MED CTR,/NASHVILLE//TN/37232; VANDERBILT INGRAM CANC CTR,/NASHVILLE//TN/37232; SUGEN INC,/S SAN FRANCISCO//CA/94080

Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 2000, V97, N17 (AUG 15), P9609-9614

ISSN: 0027-8424    Publication date: 20000815

Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418

Language: English    Document Type: ARTICLE

Abstract: Overexpression of ErbB-2/Neu has been causally associated with mammary epithelial transformation. Here we report that blockade of the epidermal growth factor receptor (EGFR) kinase with AG-1478 markedly delays breast tumor formation in mouse mammary tumor virus (MMTV)/Neu + MMTV/transforming growth factor alpha bigenic mice. This delay was associated with inhibition of EGFR and Neu signaling, reduction of cyclin-dependent kinase 2 (Cdk2) and mitogen-activated protein kinase (MAPK) activities and cyclin D1, and an increase in the levels of the Cdk inhibitor p27(Kip1). In addition, BrdUrd incorporation into tumor cell nuclei was prevented with no signs of tumor cell apoptosis. These observations prompted us to investigate the stability of p27. Recombinant p27 was degraded rapidly in vitro by untreated but not by AG-1478-treated tumor lysates. Proteasome depletion of the tumor lysates, addition of the specific MEK1/2 inhibitor U-0126, or a T187A mutation in recombinant p27 all prevented p27 degradation. Cdk2 and MAPK precipitates from untreated tumor lysates phosphorylated recombinant wild-type p27 but not the T187A mutant in vitro. Cdk2 and MAPK precipitates from AG-1478-treated tumors were unable to phosphorylate p27 in vitro. These data suggest that increased signaling by ErbB receptors up-regulates MAPK activity, which, in turn, phosphorylates and destabilizes p27, thus contributing to dysregulated cell cycle progression.

, 2000

...Abstract: p27, Recombinant p27 was degraded rapidly in vitro by untreated but not by AG-1478-treated tumor lysates, Proteasome depletion of the tumor lysates, addition of the specific MEK1/2 inhibitor U-0126, or a T187A mutation in recombinant p27 all prevented p27 degradation. Cdk2 and MAPK precipitates...

...p27 but not the T187A mutant in vitro. Cdk2 and MAPK precipitates from AG-1478-treated tumors were unable to phosphorylate p27 in vitro. These data suggest that increased signaling by ErbB...

09/942,940

5/3,K,AB/27 (Item 4 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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10355738 PMID: 7858416

Protein kinases in normal and transformed melanocytes.

Quong R Y; Bickford S T; Ing Y L; Terman B; Herlyn M; Lassam N J  
Department of Medicine, University of Toronto, Ontario, Canada.

Melanoma research (ENGLAND) Oct 1994, 4 (5) p313-9, ISSN

0960-8931 Journal Code: 9109623

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Aberrant function of protein kinases has been implicated in the development of **melanoma**. In an effort to define the molecular events involved in initiation and progression of this malignancy, we used RT-PCR to identify protein kinases in both normal and transformed melanocytes. Collectively, we identified seven clones corresponding to previously characterized protein kinases (JAK-1, TYK02, AXL/UFO, IGF1-R, KDR and FER) as well as the recently identified MLK-3/PTK1 protein kinase. Northern analysis was used to determine the expression pattern of each protein kinase in both normal melanocytes and a variety of **melanoma** cell lines. Relatively abundant levels of UFO/AXL and KDR mRNAs were observed in a subset of the **melanoma** cell lines whereas most of the remaining protein kinases were expressed at similar levels in both normal and transformed melanocytes.

✓ seal away

need seal

(+ melanoma  
and + 3 clonined cpds

+ colon cancer  
& 3 clonined cpd) to see the degree of  
cell killing -

13745003 PMID: 9440696

MAP kinase links the transcription factor Microphthalmia to c-Kit signalling in melanocytes.

Hemesath T J; Price E R; Takemoto C; Badalian T; Fisher D E

Division of Pediatric Hematology/Oncology, Children's Hospital and Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115, USA.

Nature (ENGLAND) Jan 15 1998, 391 (6664) p298-301, ISSN

0028-0836 Journal Code: 0410462

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Germline mutations at loci encoding the transcription factor Microphthalmia (Mi), the cytokine receptor c-Kit, or its ligand Steel factor (Sl) result in strikingly similar defects in mast cell and melanocyte development. Here we describe a biochemical link between Kit signalling and the activity of Mi. Stimulation of melanoma cells with Sl results in activation of MAP kinase, which in turn phosphorylates Mi at a consensus target serine. This phosphorylation upregulates Mi transactivation of the tyrosinase pigmentation gene promoter. In addition to modulating pigment production, such signalling may regulate the expression of genes essential for melanocyte survival and development. The pathway represents a new application of the general MAP kinase machinery in transducing a signal between a tissue-specific receptor at the cell surface and a tissue-specific transcription factor in the nucleus.

0008924896 BIOSIS NO.: 199396089312

Candidate metastasis-associated genes of the rat 13762NF mammary adenocarcinoma

AUTHOR: Pencil S D; Toh Y; Nicolson G L (Reprint)

AUTHOR ADDRESS: Dep. Tumor Biol., Univ. Tex. M.D. Anderson Cancer Cent.,  
1515 Holcombe Blvd., Houston, TX 77030, USA\*\*USA

JOURNAL: Breast Cancer Research and Treatment 25 (2): p165-174 1993

ISSN: 0167-6806

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Differential hybridization was used to isolate genes potentially involved in the process of metastasis. Ten complementary DNAs (cDNAs) that were differentially expressed between a highly metastatic (MTLn3) and a nonmetastatic (MTC.4) line of the rat 13762NF mammary adenocarcinoma were isolated and sequenced. Examination of the EMBL/GenBank database revealed that one of the genes had a high degree of homology (98.8%) to annexin I (also known as calpactin II). Quantitative analysis of Northern blot hybridizations showed that the annexin I-like sequence was expressed 4- to 7-fold higher in MTLn3 than in MTC.4 cells. Steady state mRNA levels were also low in MTLn2, a cell line of low metastatic potential closely related to MTLn3, but were not related to metastatic potential in colon adenocarcinoma or melanoma cells. Two of the cDNAs (designated 8.11 and 10.14) were found to be novel. The expression of 10.14 mRNA (3.2 kb) was 4-fold higher in MTLn3 than in MTC.4 cells. Sequencing of the 10.14 cDNA (2.2 kb) revealed a putative open reading frame of 583 amino acids that was also novel. Expression of 8.11 mRNA (gt 7 kb) inversely correlated with metastatic potential. Another differentially transcribed gene was highly homologous to ERK2 (extracellular signal related kinase 2), a mitogen-activated protein kinase (MAPK). Northern analysis of ERK2 expression revealed 3-fold higher amounts of a 1.3 kb mRNA in MTLn3 than in MTC.4 cells. Higher levels of ERK2 mRNA were generally seen in the more metastatic human colon but not in melanoma cell lines. We also corroborated the work of Taniguchi (Nucl Acids Res 19:6949, 1991) by independently identifying EF-1-alpha as a putative metastasis-associated gene.

#### 1993

...ABSTRACT: closely related to MTLn3, but were not related to metastatic potential in colon adenocarcinoma or melanoma cells. Two of the cDNAs (designated 8.11 and 10.14) were found to be...

...was highly homologous to ERK2 (extracellular signal related kinase 2), a mitogen-activated protein kinase (MAPK). Northern analysis of ERK2 expression revealed 3-fold higher amounts of a 1.3 kb...

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008936809 BIOSIS NO.: 199396101225

Oncostatin-M stimulates tyrosine protein phosphorylation in parallel with the activation of p42-MAPK/ERK-2 in Kaposi's cells: Evidence that this pathway is important in Kaposi cell growth

AUTHOR: Amaral Mary Catherine; Miles Steve; Kumar Gita; Nel Andre E (Reprint)

AUTHOR ADDRESS: Div. Clin. Immunol. and Allergy, Dep. Med., UCLA Sch. Med., 52-175 CHS, Los Angeles, CA 90024-1680, USA\*\*USA

JOURNAL: Journal of Clinical Investigation 92 (2): p848-857 1993

ISSN: 0021-9738

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Oncostatin-M (OSM) is a potent mitogen for Kaposi's sarcoma (KS) cells. We studied signaling by the OSM receptor in three AIDS-related KS lines and show induction of tyrosine phosphorylation of 145-, 120-, 85-, and 42-kD substrates. The 42-kD substrate was identified as p42-MAPK (mitogen-activated protein kinase), also known as ERK-2. This serine/threonine kinase relays mitogenic signals from receptor tyrosine protein kinases (TPKs) or receptor-associated TPKs to transcriptional activators. The OSM dose dependence for MAP kinase activation and induction of KS cell growth were almost identical, suggesting functional linkage. MAP kinase activation was dependent on tyrosine phosphorylation, and both OSM-induced MAP kinase activity and KS cell growth could be suppressed by TPK inhibitors, genistein and geldanamycin. OSM also stimulated tyrosine phosphorylation of similar substrates and MAP kinase activity in human vein endothelial cells. While it has been proposed that the OSM receptor may include the gp130 subunit of the IL-6 receptor and alpha-chain of leukemia inhibitory factor (LIF) receptor, neither LIF nor r.IL-6 induced tyrosine protein phosphorylation or p42-MAPK activation in KS cells. However, r.IL-6 did stimulate tyrosine phosphorylation and p42-MAPK activity in the human B cell line, AF-10, while OSM and LIF exerted no effects. Our results indicate that, although the OSM and IL-6 receptors share a common signaling pathway, this pathway is selectively activated by OSM in Kaposi's cells.

Oncostatin-M stimulates tyrosine protein phosphorylation in parallel with the activation of p42-MAPK/ERK-2 in Kaposi's cells: Evidence that this pathway is important in Kaposi cell growth

1993

...ABSTRACT: 145-, 120-, 85-, and 42-kD substrates. The 42-kD substrate was identified as p42-MAPK (mitogen-activated protein kinase), also known as ERK-2. This serine/threonine kinase relays mitogenic signals from receptor tyrosine protein kinases (TPKs) or...

...factor (LIF) receptor, neither LIF nor r.IL-6 induced tyrosine protein phosphorylation or p42-MAPK activation in KS cells. However, r.IL-6 did stimulate tyrosine phosphorylation and p42-MAPK activity in the human B cell line, AF-10, while OSM and LIF exerted no...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...MALIGNANT MELANOMA;

5/3,K,AB/23 (Item 23 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)

0009012578 BIOSIS NO.: 199497033863

Novel and known protein tyrosine kinases and their abnormal expression in human **melanoma**

AUTHOR: Easty David J (Reprint); Ganz Sue E; Farr Christine J; Lai Cary; Herlyn Meenhard; Bennett Dorothy C

AUTHOR ADDRESS: St. George's Hosp. Med. Sch., LON SW17 ORE, UK\*\*UK

JOURNAL: Journal of Investigative Dermatology 101 (5): p679-684 1993

1993

ISSN: 0022-202X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: We have used the polymerase chain reaction and Northern blotting to identify protein tyrosine kinases that may play an important role in the process of **melanoma** initiation and progression. Degenerate primers from the conserved catalytic domain of tyrosine kinase genes were used to amplify and clone partial cDNA sequences from a human **melanoma** cell line (DX3-LT5.1) and normal human melanocytes. When the **melanoma** reaction products were sequenced, 13 distinct clones were found, of which one is novel to date and has provisionally been named **MEK** (for melanocytic kinase). Of the remaining 12 known kinases, only two, **ERB-B2** and **IGF1-R**, have previously been reported in pigment cells. Reaction products from melanocytes included only eight of these 13 sequences. To test for quantitative differences in tyrosine kinase expression between normal and malignant cells, a panel of eight **melanoma** lines and normal melanocytes was analyzed by Northern blotting. Two tyrosine kinases (**JTK-14/TIE** and **TYRO-9**) were detected in some melanomas but were not found in normal melanocytes, whereas others, including **MEK**, appeared to be overexpressed in some malignant lines. A minority of kinases showed either no change or a reduction in the level of mRNA. Expression of tyrosine kinases varied independently, and individual lines contained various combinations of these enzymes. Our findings are consistent with an increased overall expression of these putative growth factor receptors during **melanoma** development.

Novel and known protein tyrosine kinases and their abnormal expression in human **melanoma**

1993

...ABSTRACT: to identify protein tyrosine kinases that may play an important role in the process of **melanoma** initiation and progression. Degenerate primers from the conserved catalytic domain of tyrosine kinase genes were used to amplify and clone partial cDNA sequences from a human **melanoma** cell line (DX3-LT5.1) and normal human melanocytes. When the **melanoma** reaction products were sequenced, 13 distinct clones were found, of which one is novel to date and has provisionally been named **MEK** (for melanocytic kinase). Of the remaining 12 known kinases, only two, **ERB-B2** and **IGF1...**

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...findings are consistent with an increased overall expression of these putative growth factor receptors during **melanoma** development.

5/3,K,AB/22 (Item 22 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
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0008936809 BIOSIS NO.: 199396101225

Oncostatin-M stimulates tyrosine protein phosphorylation in parallel with  
the activation of p42-**MAPK/ERK**-2 in Kaposi's cells: Evidence  
that this pathway is important in Kaposi cell growth

Mitogen-activated protein kinase pathway and AP-1 are activated during  
cAMP-induced melanogenesis in B-16 **melanoma** cells  
AUTHOR: Englaro Walter; Rezzonico Roger; Durand-Clement Monique; Lallemand  
Dominique; Ortonne Jean-Paul; Ballotti Robert (Reprint)  
AUTHOR ADDRESS: Inst. National Sante Recherche Medicale U385, Avenue  
Valombrose, 06107 Nice Cedex 02, France\*\*France  
JOURNAL: Journal of Biological Chemistry 270 (41): p24315-24320 1995  
1995  
ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: In mammalian melanocytes, melanin synthesis is controlled by tyrosinase, the critical enzyme in the melanogenic pathway. We and others showed that the stimulation of melanogenesis by cAMP is due to an increased tyrosinase expression at protein and mRNA levels. However, the molecular events connecting the rise of intracellular cAMP and the increase in tyrosinase activity remain to be elucidated. In this study, using B16 **melanoma** cells, we showed that cAMP-elevating agents stimulated mitogen-activated protein (MAP) kinase, p44-**mapk**. This effect was mediated by the activation of MAP kinase kinase. cAMP-elevating agents induced a translocation of p44-**mapk** to the nucleus and an activation of the transcription factor AP-1. cAMP-induced AP-1 contained FOS-related antigen-2 in association with JunD, while after phorbol ester stimulation AP-1 complexes consist mainly of JunD/c-Fos heterodimers. In an attempt to connect these molecular events to the control of tyrosinase expression that appears to be the pivotal point of melanogenesis regulation, we hypothesized that following its activation by cAMP, p44-**mapk** activates AP-1. Then AP-1 could stimulate tyrosinase expression through the interaction with specific DNA sequences present in the mouse tyrosinase promoter.

0010602555 BIOSIS NO.: 199699236615

Schiff base forming drugs: Mechanisms of immune potentiation and therapeutic potential

AUTHOR: Chen H; Rhodes J (Reprint)

AUTHOR ADDRESS: Immunol. Unit, Glaxo Wellcome Res. Dev., Med. Res. Cent., Gunnels Wood Rd., Stevenage, Hertfordshire SG1 2NY, UK\*\*UK

JOURNAL: Journal of Molecular Medicine (Berlin) 74 (9): p497-504 1996

1996

ISSN: 0946-2716

DOCUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract

LANGUAGE: English

*Feel away*

ABSTRACT: CD4 T-lymphocytes, which orchestrate immune responses, receive a cognitive signal when clonally distributed receptors are occupied by MHC class II bound peptides on antigen-presenting cells. The latter provide costimulatory or accessory signals through macromolecules such as B7.1 and B7.2 which interact with coreceptors on T-cells to regulate outcomes in terms of T-cell activation or specific non-responsiveness. Complementary studies at the chemical level have implicated Schiff base formation between specialised carbonyls and amines, constitutively expressed on antigen-presenting cell and T-cell surfaces, as an essential element in specific T-cell activation. The small xenobiotic Schiff base forming molecule tucaresol, which substitutes for the physiological donor of carbonyl groups to provide a costimulatory signal to CD4 T-helper lymphocytes (Th-cells), has been developed for testing as an immunopotentiatory drug. Tucaresol, which is orally bioavailable and systemically active, enhances CD4 Th-cell and CD8 cytotoxic T-cell responses in vivo and selectively favours a Th1-type profile of cytokine production. In murine models of virus infection and syngeneic tumour growth it has substantial therapeutic activity. Schiff base formation by tucaresol on T-cell surface amines provides a costimulatory signal to the T-cell through a mechanism that activates clofilium-sensitive K<sup>+</sup> and Na<sup>+</sup> transport. The signalling pathway utilised by tucaresol converges with T-cell receptor signalling at the level of MAP kinase, promoting the tyrosyl phosphorylation of ERK2 by MEK (mitogen-activated protein kinase kinase). The Schiff base forming class of immunopotentiatory drug provides the first orally active, mechanism-based immunopotentiatory agents for therapeutic testing. Tucaresol is currently undergoing pilot phase I/II clinical trials as an immunopotentiator in chronic hepatitis B virus infection, HIV infection and malignant melanoma.

1996

...ABSTRACT: receptor signalling at the level of MAP kinase, promoting the tyrosyl phosphorylation of ERK2 by **MEK** (mitogen-activated protein kinase kinase). The Schiff base forming class of immunopotentiatory drug provides the...

...clinical trials as an immunopotentiator in chronic hepatitis B virus infection, HIV infection and malignant melanoma.

DESCRIPTORS:

MISCELLANEOUS TERMS: ...MALIGNANT MELANOMA;

5/3,K,AB/19 (Item 19 from file: 55)

DIALOG(R)File 55:Biosis Previews(R)

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0010279385 BIOSIS NO.: 199698747218

Different mechanisms are responsible for c-jun mRNA induction by cisplatin and ultraviolet light

AUTHOR: Rabo Ylva Bendix; Shoshan Maria C; Linder Stig; Hansson Johan (Reprint)

AUTHOR ADDRESS: Dep. Oncol., Radiumhemmet, Karolinska Inst. Hosp., S-171 76  
Stockholm, Sweden\*\*Sweden  
JOURNAL: International Journal of Cancer 65 (6): p821-826 1996 1996  
ISSN: 0020-7136  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Ultraviolet light (UV) and different DNA-damaging agents are known to induce AP-I-transcription-factor activity. Whereas UV induction appears to be triggered by events at the cell membrane, the mechanism of AP-I activation by alkylating or platinating agents is not known. We have here examined the effect of cisplatin on AP-I activity in RPMI-8322 melanoma cells. Cisplatin was found to induce binding of nuclear proteins to TRE elements from the c-jun and collagenase-gene promoters, and was also found to induce activation of a c-jun-promoter reporter construct. Compared with stimulation by UV, cisplatin stimulation of c-jun-promoter activity was found to be less sensitive to a dominant negative mutant of Raf-I protein kinase. Furthermore, whereas UV treatment resulted in strong MAP-kinase activation, cisplatin treatment resulted only in a weak and transient increase. These data suggest that the Raf-MAPK pathway is of minor importance for the induction of

0011431983 BIOSIS NO.: 199800226230

Inhibition of the mitogen-activated protein kinase pathway triggers B16  
**melanoma** cell differentiation

AUTHOR: Englaro Walter; Bertolotto Corine; Busca Roser; Brunet Anne; Pages  
Gilles; Ortonne Jean-Paul; Ballotti Robert (Reprint)

AUTHOR ADDRESS: INSERM U-385, Fac. de Medecine, Avenue de Valombrosse,  
06107 Nice Cedex 2, France\*\*France

JOURNAL: Journal of Biological Chemistry 273 (16): p9966-9970 April 17,  
1998 1998

MEDIUM: print

ISSN: 0021-9258

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: In B16 **melanoma** cells, mitogen-activated protein (MAP)  
kinases are activated during cAMP-induced melanogenesis (Englaro, W.,  
Rezzonico, R., Durand-Clement, M., Lallemand, D., Ortonne, J. P., and  
Ballotti, R. (1995) J. Biol. Chem. 270, 24315-24320). To establish the  
role of the MAP kinases in melanogenesis, we studied the effects of a  
specific MAP kinase kinase (**MEK**) inhibitor PD 98059 on different  
melanogenic parameters. We showed that PD 98059 inhibits the activation  
of MAP kinase extracellular signal-regulated kinase 1 by cAMP, but does  
not impair the effects of cAMP either on the morphological  
differentiation, characterized by an increase in dendrite outgrowth, or  
on the up-regulation of tyrosinase that is the key enzyme in  
melanogenesis. On the contrary, PD 98059 promotes by itself cell  
dendricity and increases the tyrosinase amount and activity. Moreover,  
down-regulation of the MAP kinase pathway by PD 98059, or with dominant  
negative mutants of p21ras and **MEK**, triggers a stimulation of the  
tyrosinase promoter activity and enhances the effect of cAMP on this  
parameter. Conversely, activation of the MAP kinase pathway, using  
constitutive active mutants of p21ras and **MEK**, leads to an  
inhibition of basal and cAMP-induced tyrosinase gene transcription. These  
results demonstrate that the MAP kinase pathway activation is not  
required for cAMP-induced melanogenesis. Furthermore, the inhibition of  
this pathway induces B16 **melanoma** cell differentiation, while a  
sustained activation impairs the melanogenic effect of cAMP-elevating  
agents.

Inhibition of the mitogen-activated protein kinase pathway triggers B16  
**melanoma** cell differentiation

1998

ABSTRACT: In B16 **melanoma** cells, mitogen-activated protein (MAP)  
kinases are activated during cAMP-induced melanogenesis (Englaro, W.,  
Rezzonico...

...the MAP kinases in melanogenesis, we studied the effects of a specific  
MAP kinase kinase (**MEK**) inhibitor PD 98059 on different melanogenic  
parameters. We showed that PD 98059 inhibits the activation...

Glycoprotein glycosylation and cancer progression

AUTHOR: Dennis James W (Reprint); Granovsky Maria; Warren Charles E  
AUTHOR ADDRESS: Samuel Lunenfeld Research Institute, Mount Sinai Hospital,  
600 University Ave., Rm. 876, M5G 1X5, Toronto, Ont., Canada\*\*Canada  
JOURNAL: Biochimica et Biophysica Acta 1473 (1): p21-34 Dec. 6, 1999

1999  
MEDIUM: print

ISSN: 0006-3002

DOCUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Glycosylation of glycoproteins and glycolipids is one of many molecular changes that accompany malignant transformation. GlcNAc-branched N-glycans and terminal Lewis antigen sequences have been observed to increase in some cancers, and to correlate with poor prognosis. Herein, we review evidence that beta1,6GlcNAc-branching of N-glycans contributes directly to cancer progression, and we consider possible functions for the glycans. Mgat5 encodes N-acetylglucosaminyltransferase V (GlcNAc-TV), the Golgi enzyme required in the biosynthesis of beta1,6GlcNAc-branched N-glycans. Mgat5 expression is regulated by RAS-RAF-MAPK, a signaling pathway commonly activated in tumor cells. Ectopic expression of GlcNAc-TV in epithelial cells results in morphological transformation and tumor growth in mice, and over expression in carcinoma cells has been shown to induce metastatic spread. Ectopic expression of GlcNAc-TIIII, an enzyme that competes with GlcNAc-TV for acceptor, suppresses metastasis in B16 melanoma cells. Furthermore, breast cancer progression and metastasis induced by a viral oncogene expressed in transgenic mice is markedly suppressed in a GlcNAc-TV-deficient background. Mgat5 gene expression and beta1,6GlcNAc-branching of N-glycans are associated with cell motility, a required phenotype of malignant cells.

1999

...ABSTRACT: the biosynthesis of beta1,6GlcNAc-branched N-glycans. Mgat5 expression is regulated by RAS-RAF-MAPK, a signaling pathway commonly activated in tumor cells. Ectopic expression of GlcNAc-TV in epithelial...

...GlcNAc-TIIII, an enzyme that competes with GlcNAc-TV for acceptor, suppresses metastasis in B16 melanoma cells. Furthermore, breast cancer progression and metastasis induced by a viral oncogene expressed in transgenic...

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...RAS-RAF-MAPK;

5/3,K,AB/16 (Item 16 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
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0011688763 BIOSIS NO.: 199800483010

Activation of JNK and p38 but not ERK MAP kinases in human skin cells  
by 5-aminolevulinate-photodynamic therapy

AUTHOR: Klotz Lars-Oliver; Fritsch Clemens; Briviba Karlis; Tsacmacidis

5/3,K,AB/14 (Item 14 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
(c) 2005 BIOSIS. All rts. reserv.

0012364269 BIOSIS NO.: 200000082582

B-Raf mediates the cAMP activation of **MAPK** in B16 melanoma cells

AUTHOR: Busca Roser (Reprint); Abbe Patricia (Reprint); Mantoux Frederic (Reprint); Aberdam Edith (Reprint); Eychene Alain; Ortonne Jean-Paul (Reprint); Ballotti Robert (Reprint)

AUTHOR ADDRESS: INSERM U385, Avenue Valombrose, 06107, Nice, France\*\*France

JOURNAL: Pigment Cell Research (SUPPL. 7): p73 1999 **1999**

MEDIUM: print

CONFERENCE/MEETING: XVIIth International Pigment Cell Conference Nagoya, Japan October 30-November 3, 1999; 19991030

ISSN: 0893-5785

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Citation

LANGUAGE: English

B-Raf mediates the cAMP activation of **MAPK** in B16 melanoma cells

**1999**

DESCRIPTORS:

...ORGANISMS: **melanoma** cells

0012468470 BIOSIS NO.: 2000000186783

Synergistic anti-tumoral effect of paclitaxel (Taxol)+AS101 in a murine model of B16 **melanoma**: Association with ras-dependent signal-transduction pathways

AUTHOR: Kalechman Yona; Longo Dan L; Catane Raphael; Shani Adi; Albeck Michael; Sredni Benjamin (Reprint)

AUTHOR ADDRESS: Faculty of Life Sciences, C.A.I.R. Institute, Bar Ilan University, Ramat Gan, 52900, Israel\*\*Israel

JOURNAL: International Journal of Cancer 86 (2): p281-288 April 15, 2000 2000

MEDIUM: print

ISSN: 0020-7136

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Optimal doses of paclitaxel (Taxol) combined with the immunomodulator AS101, previously shown to have antitumoral effects, administered to B16 **melanoma**-bearing mice decreased tumor volume and resulted in over 60% cure. Paclitaxel+AS101 directly inhibited the clonogenicity of B16 **melanoma** cells in a synergistic, dose-dependent manner. We suggest that this results from both reduced paclitaxel-induced bone marrow toxicity and induction of differential signal-transduction pathways, which lead to apoptosis of tumor cells. Paclitaxel+AS101 synergistically activated c-raf-I and **MAPK** ERK1 and ERK2. This activation was essential for the synergistic induction of p21waf protein. Cell-cycle analysis of B16 cells treated with both compounds revealed an increased accumulation in G2M, though AS101 alone produced significant G1 arrest. These activities were ras-dependent. AS101+paclitaxel induced significant synergistic phosphorylation (inactivation) of the anti-apoptotic protein Bcl-2. Whereas phosphorylation of Bcl-2 by paclitaxel was raf-dependent only, the synergistic effect of both compounds together was ras-, raf- and **MAPK**-dependent. No effect of the combined treatment on Bax protein expression was observed. We suggest that AS101 renders more cells susceptible to Bcl-2 phosphorylation by paclitaxel, possibly by increasing the accumulation of paclitaxel-induced cells in G2M. Exposure of B16 cells to clinically achievable concentrations of paclitaxel+AS101 increased the rate of apoptosis of treated cells. Apoptosis induced by AS101 alone was both raf- and **MAPK**-dependent, while that induced by paclitaxel was raf-dependent only.

Synergistic anti-tumoral effect of paclitaxel (Taxol)+AS101 in a murine model of B16 **melanoma**: Association with ras-dependent signal-transduction pathways

2000

...**ABSTRACT:** Taxol) combined with the immunomodulator AS101, previously shown to have antitumoral effects, administered to B16 **melanoma**-bearing mice decreased tumor volume and resulted in over 60% cure. Paclitaxel+AS101 directly inhibited the clonogenicity of B16 **melanoma** cells in a synergistic, dose-dependent manner. We suggest that this results from both reduced...

...which lead to apoptosis of tumor cells. Paclitaxel+AS101 synergistically activated c-raf-I and **MAPK** ERK1 and ERK2. This activation was essential for the synergistic induction of p21waf protein. Cell...

...was raf-dependent only, the synergistic effect of both compounds together was ras-, raf- and **MAPK**-dependent. No effect of the combined treatment on Bax protein expression was observed. We suggest...

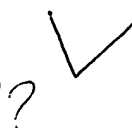
...rate of apoptosis of treated cells. Apoptosis induced by AS101 alone was both raf- and **MAPK**-dependent, while that induced by paclitaxel was

raf-dependent only.

DESCRIPTORS:

DISEASES: B-16 melanoma--

Anti-apoptotic defenses in melanoma are regulated through multiple  
signaling pathways including Ras, PI3K, ~~MEK~~ and NF-kB  
AUTHOR: Shellman Y (Reprint); Gendall J (Reprint); Weston W (Reprint); Marr  
D (Reprint); Maxwell I (Reprint); Norris D A (Reprint)  
AUTHOR ADDRESS: Department of Dermatology, University of Colorado Health  
Science Center, Denver, CO, USA\*\*USA  
JOURNAL: Journal of Investigative Dermatology 114 (4): p789, April, 2000  
2000  
MEDIUM: print  
CONFERENCE/MEETING: 61st Annual Meeting of the Society for Investigative  
Dermatology. Chicago, Illinois, USA May 10-14, 2000; 20000510  
ISSN: 0022-202X  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Citation  
LANGUAGE: English



Ras mediates the cAMP-dependent activation of extracellular  
signal-regulated kinases (ERKs) in melanocytes

AUTHOR: Busca Roser (Reprint); Abbe Patricia; Mantoux Frederic; Aberdam  
Edith; Peyssonnaud Carole; Eychene Alain; Ortonne Jean-Paul; Ballotti  
Robert

AUTHOR ADDRESS: Faculte de Medecine, INSERM U385, Avenue de Valombrose,  
06107, Nice Cedex 2, France\*\*France

JOURNAL: EMBO (European Molecular Biology Organization) Journal 19 (12): p  
2900-2910 June 15, 2000 2000

MEDIUM: print

ISSN: 0261-4189

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: In melanocytes and melanoma cells, cAMP activates  
extracellular signal-regulated kinases (ERKs) and MEK-1 by an  
unknown mechanism. We demonstrate that B-Raf is activated by cAMP in  
melanocytes. A dominant-negative mutant of B-Raf, but not of Raf-1,  
blocked the cAMP-induced activation of ERK, indicating that B-Raf  
is the MEK-1 upstream regulator mediating this cAMP effect. Studies  
using Clostridium sordelii lethal toxin and Clostridium difficile toxin B  
have suggested that Rap-1 or Ras might transduce cAMP action. We show  
that Ras, but not Rap-1, is activated cell-specifically and mediates the  
cAMP-dependent activation of ERKs, while Rap-1 is not involved in this  
process in melanocytes. Our results suggest a novel, cell-specific  
mechanism involving Ras small GTPase and B-Raf kinase as mediators of  
ERK activation by cAMP. Also, in melanocytes, Ras or ERK  
activation by cAMP is not mediated through protein kinase A activation.  
Neither the Ras exchange factor, Son of sevenless (SOS), nor the  
cAMP-responsive Rap-1 exchange factor, Epac, participate in the  
cAMP-dependent activation of Ras. These findings suggest the existence of  
a melanocyte-specific Ras exchange factor directly regulated by cAMP.

5/3,K,AB/6 (Item 6 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
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0012744680 BIOSIS NO.: 200000462993

UVB induced cell cycle checkpoints in an early stage human melanoma  
line, WM35

AUTHOR: Petrocelli T; Slingerland J (Reprint)

AUTHOR ADDRESS: Division of Biology Research, Sunnybrook and Women's  
College Health Sciences Centre, 2075 Bayview Avenue, Research Building,  
S-218, Toronto, ON, M4N 3M5, Canada\*\*Canada

JOURNAL: Oncogene 19 (39): p4480-4490 14 September, 2000 2000

MEDIUM: print

ISSN: 0950-9232

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The activation of cell cycle checkpoints in response to genotoxic stressors is essential for the maintenance of genomic integrity. Although most prior studies of cell cycle effects of UV irradiation have used UVC, this UV range does not penetrate the earth's atmosphere. Thus, we have investigated the mechanisms of ultraviolet B (UVB) irradiation-induced cell cycle arrest in a biologically relevant target cell type, the early stage human melanoma cell line, WM35. Irradiation of WM35 cells with UVB resulted in arrests throughout the cell cycle: at the G1/S transition, in S phase and in G2. G1 arrest was accompanied by increased association of p21 with cyclin E/cdk2 and cyclin A/cdk2, increased binding of p27 to cyclin E/cdk2 and inhibition of these kinases. A loss of Cdc25A expression was associated with an increased inhibitory phosphotyrosine content of cyclin E- and cyclin A-associated cdk2 and may also contribute to G1 arrest following UVB irradiation. The association of Cdc25A with 14-3-3 was increased by UVB. Reduced cyclin D1 protein and increased binding of p21 and p27 to cyclin D1/cdk4 complexes were also observed. The loss of cyclin D1 could not be attributed to inhibition of either ~~MAPK~~ or PI3K/PKB pathways, since both were activated by UVB. ~~Cdc25B levels fell and the remaining protein showed an increased~~ association with 14-3-3 in response to UVB. Losses in cyclin B1 expression and an increased binding of p21 to cyclin B1/cdk1 complexes also contributed to inhibition of this kinase activity, and G2/M arrest.

UVB induced cell cycle checkpoints in an early stage human melanoma  
line, WM35

2000

...ABSTRACT: induced cell cycle arrest in a biologically relevant target cell type, the early stage human melanoma cell line, WM35. Irradiation of WM35 cells with UVB resulted in arrests throughout the cell...

...also observed. The loss of cyclin D1 could not be attributed to inhibition of either ~~MAPK~~ or PI3K/PKB pathways, since both were activated by UVB. Cdc25B levels fell and the...

DESCRIPTORS:

DISEASES: melanoma--

MESH TERMS: Melanoma (MeSH)

5/3,K,AB/5 (Item 5 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
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0012812443 BIOSIS NO.: 200000530756  
Overexpression of Ras-independent c-Raf-1 suppresses invasion of human A375  
melanoma

AUTHOR: Ge Xiaokang (Reprint); Fu Ya-Ming (Reprint); Li Yi-Qi (Reprint);  
Meadows Gary G (Reprint)

AUTHOR ADDRESS: Department of Pharmaceutical Sciences, College of Pharmacy,  
and the Cancer Prevention and Research Center, Washington State  
University, Pullman, WA, 99164-6534, USA\*\*USA

JOURNAL: International Journal of Molecular Medicine 6 (Supplement 1): p  
S32 2000 2000

MEDIUM: print

CONFERENCE/MEETING: Joint Meeting of the 5th World Congress on Advances in  
Oncology and the 3rd International Symposium on Molecular Medicine Crete,  
Greece October 19-21, 2000; 20001019

ISSN: 1107-3756

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Overexpression of Ras-independent c-Raf-1 suppresses inv

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? s mapk or erk or mek  
22315 MAPK  
19372 ERK  
9336 MEK  
S1 39085 MAPK OR ERK OR MEK

? s melanoma  
S2 102795 MELANOMA

? s s1 and s2  
39085 S1  
102795 S2  
S3 339 S1 AND S2

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339 S3  
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>>>Duplicate detection is not supported for File 340.

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